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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)	
	10/588,011	ANDERSSON, KARL	
Office Action Summary	Examiner	Art Unit	
	ANN Y. LAM	1641	
The MAILING DATE of this communication a Period for Reply	appears on the cover sheet w	th the correspondence address	
A SHORTENED STATUTORY PERIOD FOR REF WHICHEVER IS LONGER, FROM THE MAILING - Extensions of time may be available under the provisions of 37 CFR after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory perion. - Failure to reply within the set or extended period for reply will, by stat Any reply received by the Office later than three months after the may earned patent term adjustment. See 37 CFR 1.704(b).	DATE OF THIS COMMUNION 1.136(a). In no event, however, may a solution of will apply and will expire SIX (6) MON tute, cause the application to become AF	CATION. eply be timely filed THS from the mailing date of this communication. EANDONED (35 U.S.C. § 133).	
Status			
Responsive to communication(s) filed on 22 This action is FINAL . 2b) ☑ TI Since this application is in condition for allow closed in accordance with the practice unde	his action is non-final. vance except for formal matt	·	
Disposition of Claims			
4) Claim(s) <u>1-20</u> is/are pending in the application 4a) Of the above claim(s) is/are with description 5) Claim(s) is/are allowed. 6) Claim(s) <u>1-20</u> is/are rejected. 7) Claim(s) is/are objected to. 8) Claim(s) are subject to restriction and application Papers 9) The specification is objected to by the Examination	rawn from consideration.		
10) The drawing(s) filed on is/are: a) a Applicant may not request that any objection to the Replacement drawing sheet(s) including the correct and the	he drawing(s) be held in abeyar ection is required if the drawing	ce. See 37 CFR 1.85(a). (s) is objected to. See 37 CFR 1.121(d).	
Priority under 35 U.S.C. § 119			
 12) Acknowledgment is made of a claim for forei a) All b) Some * c) None of: 1. Certified copies of the priority docume 2. Certified copies of the priority docume 3. Copies of the certified copies of the priority docume application from the International Bure * See the attached detailed Office action for a limit 	ents have been received. ents have been received in A riority documents have been eau (PCT Rule 17.2(a)).	pplication No received in this National Stage	
Attachment(s) 1) Notice of References Cited (PTO-892) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date	Paper No(Summary (PTO-413) s)/Mail Date nformal Patent Application 	

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17, line 8, recite "the cell dish support". The claim lacks antecedent basis for this limitation. Applicant argues that the antecedent support is found in the parent claim 2, which recites that the support is an essentially flat dish. This is not persuasive since the two are not equivalents. A cell dish support is not necessarily a flat dish, and a flat dish is not necessarily a cell dish support.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 and 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wigstrom et al. 20040181343.

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Wigstrom et al. disclose that a microfluidic chip typically comprises a plurality of microchannels through which picoliter-to-nanoliter volumes of solvent, sample, and reagents solutions progress through narrow tunnels to be mixed, separated, and/or analyzed. See paragraph 94. Wigstrom et al. also disclose that a "microfluidic substrate", which refers to a substrate that comprises at least one microchannel, can be planar, but may be of any shape, including circular. The substrate may also have interconnecting element(s) for interfacing the microfluidic substrate with a macroscale component. See paragraph 68. Wigstrom et al. further disclose a "sensor chamber" which receives sensors and comprise outlets in one or more walls from at least two microchannels. The sensor chamber can for example be cylindrical (e.g., when the chamber is discshaped). One or more wall(s) and/or base can be optically transmissive. See paragraph 69. The "sensors" comprise molecules immobilized on a substrate, wherein the molecules are capable of producing a measurable response upon interacting with a compound which binds to the molecules. See paragraph 70. Such molecules can be nucleic acids or peptides and cells. See paragraph 228. Wigstrom et al. also teach scanning of the substrate relative to one or more sensors (e.g., by moving the substrate, by moving the one or more sensors, or by moving both the substrate and one or more sensors). Movement may be in an x-, y-, and/or z-direction. Alternatively, or additionally, movement may comprise rotating and/or tilting the substrate and/or sensor. See paragraph 89. Motion along all axes can be driven by stepper motors so that precise and accurate positioning may be achieved. A servo motor or other actuator systems may be

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used for precise position control. See paragraph 173. The device has the capability of temporarily reducing in a defined area of the support of the device the amount of liquid with which the support is brought into contact in the course of a detection since the device is capable of being tilted.

It is emphasized that claim 1 is directed to a device. Thus the tilting ability of the device as discussed above meets the claimed limitation regarding "a mechanism adapted for stirring of the liquid in contact with the solid support temporarily reducing....." since the element allowing for tilting is capable of allowing for stirring [movement/mixing to any degree] of liquid in contact with the solid support and temporarily reducing, in a define areas, the amount of liquid....

Moreover, Wigstrom et al. disclose that in one example, one of the channels in the device includes agents for use as internal controls or standards. See paragraph 232. Wigstrom et al. also more generally disclose in paragraph 0077, that "a measurable response" refers to a response that differs significantly from background as determined using controls appropriate for a given technique. It is understood that the background measurable response is a negative control in which no species of interest is attached.

However, Wigstrom et al. do not disclose an embodiment which has *both* one area of the device having immobilized species and one area not have species of interest attached so as to form a reference area (negative control.)

However, given that Wigstrom et al. teach that one channel can be reserved for an internal control with known agonist (positive control), the skilled artisan would have recognized that, similarly, one channel can serve as a negative control.

As to claim 2, the disc-shape (paragraph 69) is a flat dish.

As to claim 3, movement may comprise rotating and/or tilting the substrate and/or sensor. See paragraph 89. Motion along all axes can be driven by stepper motors so that precise and accurate positioning may be achieved. A servo motor or other actuator systems may be used for precise position control. See paragraph 173..

As to claims 4, 15 and 16, a cell can be positioned in the measurement chamber using a micropositioner (which may be stationary or movable) such as a pipette, capillary, column, optical tweezer, piezoelectric cantilever systems and/or can be dispensed into a measurement chamber using a dispenser such as an nQUAD aspirate dispenser. Other methods can used to position a cell such as, suction, the use of voltage pulses (electrophoresis, dielectrophoresis, electroendoosmosis), and the like. See paragraph 133.

As to claim 12, Wigstrom et al. disclose use of the device (see discussion of claim 1), to measure a response upon immobilized molecules interacting with a compound. See paragraph 70. Such molecules can be nucleic acids or peptides and cells. See paragraph 228. Wigstrom et al. however do not teach that the amount of liquid covering the defined portion of the support is temporarily reduced prior to performing the measurement. However, Wigstrom et al. do teach that movement may comprise rotating and/or tilting the substrate and/or sensor. See paragraph 89. The skilled artisan would have recognized that this tilting can provide for a temporary reduction in the amount of liquid covering the defined portion of the support, in the case where the support or its chambers are not

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entirely filled with a fluid. It would have been within the skills of the ordinary artisan to rotate and/or tilt the substrate prior to performing the measurement since the skilled artisan would have recognized that this provides the mixing and/or contacting step required for the interaction to occur. Additionally, the skilled artisan would have also recognized that the tilting, causing fluid to be temporarily reduced in a defined portion of the substrate, may also allow for making a measurement without the sample/reagent being in contact with the portion to be detected (negative control) and for making a measurement where the sample/reagent makes contact with the region/immobilized species. It is noted that the tilting inherently stirs [moves/mixes to any degree] the liquid in contact with the solid support.

As to claim 13, Wigstrom et al. disclose use of the device (see discussion of claim 1), to measure a response upon immobilized molecules interacting with a compound. See paragraph 70. Such molecules can be nucleic acids or peptides and cells. See paragraph 228.

As to claim 14, the molecular weight of the second species depends on what type of species it is, and since Wigstrom et al. disclose that the second species in the liquid can be any of various nucleic acids or peptides and cells (see paragraph 228), the molecular weight of the second species as claimed does not render the claim unobvious.

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Claims 5 and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wigstrom et al. 20040181343, in view of Knapp et al., 6,444,461.

Wigstrom et al. has been discussed above. However, Wigstrom et al. do not teach that the detector is a scintillation detector, and wherein there is further provided an electronic counter device for counting the impulses from the detector, and a control unit for adjusting and reporting the angular position of the support, and a computer for synchronizing scintillation counter output from the counter and the angular position of the cell dish support from the control unit.

However, Wigstrom et al. do teach a computer program products for coordinating the movement of cells and other components in a microfluidic substrate with data acquisition. See paragraph 0009. In one aspect, a computer program product Is embedded in a computer readable medium, comprising instructions for controlling one or more functions of a microfluidic substrate in response to received data regarding one or more substrate properties.

Preferably, at least one of the functions comprises scanning a sensor, such as a cell, relative to an outlet of at least one microchannel in the substrate. In another aspect, the computer program product provides instructions to expose the microfluidic substrate to a plurality of interdigitating fluid streams comprising alternating streams of agent and buffer. See paragraph 0011.

The computer program product is "operably linked" to a microfluidic substrate is one which provides instructions (e.g., through a processor providing signals to the actuator) which are executed by a actuator in communication with

the substrate, which causes the substrate to execute one or more substrate functions and/or to change substrate properties in response to receipt of the instructions. See paragraph 0085. In one aspect, as shown in FIG. 1, a microfluidic workstation comprises a microfluidic substrate and a suite of computer program products for controlling and detecting processes occurring on a microfluidic substrate. See paragraph 0088. Preferably, at least one substrate function includes scanning of the substrate relative to one or more sensors (e.g., by moving the substrate, by moving the one or more sensors, or by moving both the substrate and one or more sensors, or by varying pressure in one or more channels). Movement may be in an x-, y-, and/or z-direction. Alternatively, or additionally, movement may comprise rotating and/or tilting the substrate and/or sensor. See paragraph 0080. In another aspect, the workstation further comprises a data acquisition program for storing data received from at least the application program, in a memory unit. More preferably, the data acquisition system also receives data from detection software which has received data from the one or more sensors. See paragraph 0091.

In short, Wigstrom et al. disclose operably linking the microfluidic substrate with a computer that will control the substrate and/or sensors in x-, y- and/or z-direction, and for rotating and tilting the substrate, and the computer can also receive data from the sensor, wherein the computer may cause the substrate to execute one or more substrate functions and/or to change substrate properties in response to receipt of the instructions.

Moreover, Knapp et al. teach a microfluidic device for analyzing species in an analysis region of the microfluidic device, wherein the detector can be a scintillation counting device. As an example, detection of the size separated products is used to compile sequence information for the region being sequenced. A computer is used to select a second primer from the presynthesized primer set which hybridizes to the sequenced region, and the process is iteratively repeated with the second primer, leading to sequencing of a second region, selection of a third primer hybridizing to the second region, etc. (column 14, lines 47-64.)

As to claims 17-19, it would have been obvious to one of ordinary skills in the art at the time the invention was made to providing a scintillation counting device as the specific sensor generally disclosed by Wigstrom et al. since such a sensor is a well known sensor for detecting a species, as shown by Knapp et al. The skilled artisan would have had a reasonable expectation of success because Knapp et al. disclose that a scintillation counter device can be used in conjunction with a microfluidic device, such as the Wigstrom et al. device.

It would have also been obvious to one of ordinary skill in the art at the time the invention was made to provide a computer capability that allows for the computer to control the substrate (as disclosed by Wigstrom et al.) in response to a data received from the sensor, such as the scintillation counter disclosed by Knapp et al. since Wigstrom et al. al. teach that the computer can control the positioning of the substrate based on received data, and Knapp et al. teach that a computer can control processes, e.g., selection of a primer, based on

hybridization detected. That is, the skilled artisan would have recognized that the teachings of Wigstrom et al., in using a computer to control the substrate based on received data, and Knapp et al., in using a computer to control biochemical processes in a microfluidic device based on a detection, to thereby provide a computer that will adjust the position of the Wigstrom et al. substrate, including rotation and/or tilting (i.e., angular position) as desired, e.g., for mixing, contact, removed fluid as discussed previously above (i.e., synchronizing the scintillation counter output from the counter and the angular position of the substrate). (It is noted that the Knapp et al. scintillation counter device includes an electronic counter device.)

As to claim 20, the discussion above regarding claims 6 and 7 apply here as well.

Claims 6-9 and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wigstrom et al. 20040181343, in view of Graves 4,829,009, and further in view of Merkh et al., 5,281,540.

As to claim 6, Wigstrom et al. disclose that use of a microfluidic chip typically comprises a plurality of microchannels through which picoliter-to-nanoliter volumes of solvent, sample, and reagents solutions progress through narrow tunnels to be mixed, separated, and/or analyzed. See paragraph 94. Wigstrom et al. also disclose that a "microfluidic substrate", which refers to a

substrate that comprises at least one microchannel, can be planar, but may be of any shape, including circular. The substrate may also have interconnecting element(s) for interfacing the microfluidic substrate with a macroscale component. See paragraph 68. Wigstrom et al. further disclose a "sensor chamber" which receives sensors and comprise outlets in one or more walls from at least two microchannels. The sensor chamber can for example be cylindrical (e.g., when the chamber is disc-shaped). One or more wall(s) and/or base can be optically transmissive. See paragraph 69. The "sensors" comprise molecules immobilized on a substrate, wherein the molecules are capable of producing a measurable response upon interacting with a compound which binds to the molecules. See paragraph 70. Such molecules can be nucleic acids or peptides and cells. See paragraph 228. Wigstrom et al. also teach scanning of the substrate relative to one or more sensors (e.g., by moving the substrate, by moving the one or more sensors, or by moving both the substrate and one or more sensors). Movement may be in an x-, y-, and/or z-direction. Alternatively, or additionally, movement may comprise rotating and/or tilting the substrate and/or sensor. See paragraph 89. Motion along all axes can be driven by stepper motors so that precise and accurate positioning may be achieved. A servo motor or other actuator systems may be used for precise position control. See paragraph 173. The device has the capability of temporarily reducing in a defined area of the support of the device the amount of liquid with which the support is brought into contact in the course of a detection since the device is capable of being tilted.

Moreover, Wigstrom et al. disclose that in one example, one of the channels in the device includes agents for use as internal controls or standards. See paragraph 232. Wigstrom et al. also more generally disclose in paragraph 0077, that "a measurable response" refers to a response that differs significantly from background as determined using controls appropriate for a given technique. It is understood that the background measurable response is a negative control in which no species of interest is attached.

However, Wigstrom et al. do not disclose an embodiment which has both one area of the device having immobilized species and one area not have species of interest attached so as to form a reference area (negative control.)

However, given that Wigstrom et al. teach that one channel can be reserved for an internal control with known agonist (positive control), the skilled artisan would have recognized that, similarly, one channel can serve as a negative control.

As to claims 6 and 12, Wigstrom et al. disclose use of the device (see discussion of claim 1), to measure a response upon immobilized molecules interacting with a compound. See paragraph 70. Such molecules can be nucleic acids or peptides and cells. See paragraph 228.

Wigstrom et al. however do not teach that the amount of liquid covering the defined portion of the support is temporarily reduced prior to performing the measurement. However, Wigstrom et al. do teach that movement may comprise rotating and/or tilting the substrate and/or sensor. See paragraph 89. The skilled artisan would have recognized that this tilting can provide for a temporary

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reduction in the amount of liquid covering the defined portion of the support, in the case where the support or its chambers are not entirely filled with a fluid.

The skilled artisan would have also recognized that the tilting, causing fluid to be temporarily reduced in a defined portion of the substrate, may also allow for making a measurement without the sample/reagent being in contact with the portion to be detected (negative control) and for making a measurement where the sample/reagent makes contact with the region/immobilized species.

This is also supported by the teachings of Graves that even negative samples [i.e., negative control samples] have background noise and that to determine whether there is background noise in the negative samples, the negative samples can be tested in both the detecting and control wells of the invention [i.e., the negative samples can be tested in wells with the testing reagent, and wells without the antitarget], (col. 10, lines 5-10). Graves teaches that the results should be essentially equal in both wells, which indicates that the noise signal is close or equal to zero (col. 10, lines 10-12). Graves similarly teaches this principle in column 9, lines 3-6, disclosing wells indicated as C and D, both containing essentially a negative samples and C also having the testing reagent (antitarget) and D does not (see col. 8, lines 46-50). Graves teaches that C and D should have identical readings, which indicates the balance of noise [elimination of noise], (col. 9, lines 3-5). Graves similarly teaches a corrected reading for the test sample. More specifically, Graves teaches that wells indicated as A and D, both containing target [i.e., a sample having the target to be detected], with A also having the testing reagent (antitarget) and B does not

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(col. 8, lines 45-50). Graves teaches subtracting the result obtained in B well from the result obtain in A well for a corrected reading (col. 9, lines 8-10).

Graves in short teaches that there is background noise even in control samples that should be accounted for, by determining that the result in the control sample which is contacted with a testing reagent is the same as the result in the control sample which is not contacted with the testing reagent. Graves similarly teach that the reading of the result In the assay of the test sample that is contacted with the testing reagent should be corrected by subtracting the result of an assay of the test sample that is not contacted with the testing reagent. While the assays disclosed by Graves relate to performing assays in wells, the skilled artisan would have recognized that the teachings apply to any solid support or reservoir holding the reagents and samples. It would have been obvious to one of ordinary skill in the art at the time the invention was made utilize the Wigstrom et al. device to make detections as suggested by Graves such that the detection channel is detected with materials removed from inside it. and that the tilting of the device allows for removal of the materials for detection of the channel by itself in order to detect background noise that may interfere with the assay results.

Moreover, the skilled artisan would have had reasonable expectation of success in performing the steps discussed above because the microfluidic substrate of Wigstrom et al. may include various components that allow for fluid manipulation, such as a valve (paragraph 0084).

It is noted that the tilting inherently stirs [moves/mixes to any degree] the liquid in contact with the solid support.

Moreover, a positive step of stirring, using the x-y-z positioner, including tilting, is within the skills of the ordinary artisan as it is well known that reactions are facilitated by stirring or otherwise mixing the reagents and samples for increasing contact between the materials. This is also supported by the disclosure of Merkh et al. that a device that agitates the wells of a reaction cartridge promotes faster and more complete reactions and allows the use of smaller volumes of sample and reagents (col. 6, lines 48-56.) Thus, this further supports that it would have been obvious to the skilled artisan to utilize the device disclosed by Merkh et al. including the rotating and tilting mechanism to provide for agitation for the advantages of promoting faster and more complete reactions and allowing the use of smaller volumes of sample and reagents as taught by Merkh et al.

As to claim 7, the skilled artisan would have recognized that repetition of the detection is a mechanism for observing the changes in interaction over time. The duration of time in which the repititions are made are within a workable range and thus is within the skills of the ordinary artisan.

As to claim 8, the tilting provides a temporary reduction without changing the total amount of liquid in the support.

As to claim 9, use of a control or reference measurement is discussed above regarding claim 1. Comparing or calculating a difference between target and reference measurement is a basic principle that is well known in the assay

art in order to detect a positive or negative result and/or to substract background noise.

As to claim 11, the disc-shape (paragraph 69) is a flat dish.

As to claim 13, Wigstrom et al. disclose use of the device (see discussion of claim 1), to measure a response upon immobilized molecules interacting with a compound. See paragraph 70. Such molecules can be nucleic acids or peptides and cells. See paragraph 228.

As to claim 14, the molecular weight of the second species depends on what type of species it is, and since Wigstrom et al. disclose that the second species in the liquid can be any of various nucleic acids or peptides and cells (see paragraph 228), the molecular weight of the second species as claimed does not render the claim unobvious.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wigstrom et al. 20040181343, in view of Graves 4,829,009, and Merkh et al., 5,281,540, as applied to claim 6 above, and further in view of Knapp et al., 6,444,461.

As to claim 10, Wigstrom et al. disclose that scans can be made across microfluidic channel with varying doses and that from these data, a doseresponse curve can be created for an unknown agonist. See paragraph 0047. However, Wigstrom et al. do not specifically teach that a similar assay can be

achieved by increasing the species that is exposed to the species that is immobilized in the Wigstrom et al. device. However, Knapp et al. teach, for example, subjecting a species to increasing concentrations of a material to monitor a particular characteristic (col. 35, lines 48-61.) The skilled artisan would have recognized that this same principle can be applied to increase the second species in the Wigstrom et al. device to monitor the effect, for purposes such as obtaining a dose-response curve.

Response to Arguments

Applicant's arguments have been considered but are not persuasive for the reasons set forth above.

Applicant argues that neither Wigstrom et al. nor Knapp et al. teach a structure or step for stirring. Specifically, Applicant argues that Wigstrom et al. fail to teach a mechanism or step by which the amount of liquid in a detection area is temporarily reduced in connection with a detection. It is pointed out by Applicant that the microchannels are disclosed as open-ended in paragraph 67, and a sensor is exposed to a plurality of fluid streams emerging therefrom, and thus Wigstrom et al. require that during the course of a detection at the microchannel outlets, the fluid streams flow at a uniform rate at steady state concentrations. Applicant further argues that any tilting of Wigstrom et al., whether for scanning a sensor across the emerging fluid streams or to impart flow to those streams, cannot reduce the amount of liquid during a detection because to do so would

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destroy Wigstrom's requirement that the detected fluid streams must flow at a uniform rate and steady state concentration.

These arguments are not persuasive for the following reasons.

As to the device claims, the mechanism to temporarily reduce liquid with which the support is brought into contact in the course of detection is the tilting mechanism.

As to the method claims, as stated above, the skilled artisan would have also recognized that the tilting, causing fluid to be temporarily reduced in a defined portion of the substrate, may also allow for making a measurement without the sample/reagent being in contact with the portion to be detected (negative control) and for making a measurement where the sample/reagent makes contact with the region/immobilized species.

This is also supported by the teachings of Graves that even negative samples [i.e., negative control samples] have background noise and that to determine whether there is background noise in the negative samples, the negative samples can be tested in both the detecting and control wells of the invention [i.e., the negative samples can be tested in wells with the testing reagent, and wells without the antitarget], (col. 10, lines 5-10). Thus at the least Graves disclose a motivation for detecting the channel area, drained of materials.

As to Applicant's point on the open-ended channels, this is not persuasive because the microfluidic substrate of Wigstrom et al. may include various components that allow for fluid manipulation, such as a valve (paragraph 0084).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/ Primary Examiner, Art Unit 1641 Application/Control Number: 10/588,011 Page 20

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